Remarks

Claims 1-10, 12, 14-18, 20-26, 28 and 30-41 are pending in the present application. Claim 1 has been amended. The following objections and rejections are at issue and are set forth by number in the order in which they are addressed:

1. Claims 1-10, 12, 14-18, 20-26, 28 and 30-41 are provisionally rejected for double patenting over co-pending Application No.: 11/928,464 in view of Schroder;
2. Claims 1-10, 12, 14, 18, 20, 21, 28, 30-34, and 41 are rejected under 35 U.S.C. §103, as allegedly being obvious over Mathor et al. in view of each of Felts et al.; Wang et al.; Zhou et al. and Inaba et al.;
3. Claims 1-10, 12, 14-18, 20, 21, 28, 30-34, and 41 are rejected under 35 U.S.C. §103, as allegedly being obvious over Mathor et al. in view of each of Felts et al.; Wang et al.; Zhou et al. and Inaba et al. in further view of Burns et al.;
4. Claims 1-10, 12, 14, 18, 20, 21, 26, 28, 30-38 and 41 are rejected under 35 U.S.C. §103, as allegedly being obvious over Mathor et al. in view of each of Felts et al.; Wang et al.; Zhou et al. and Inaba et al., in further view of Schroder et al.;
5. Claims 1-10, 12, 14, 18, 20-24, 26, 28, 30-34, and 39-41 are rejected under 35 U.S.C. §103, as allegedly being obvious over Mathor et al. in view of each of Felts et al.; Wang et al.; Zhou et al. and Inaba et al. in further view of Primus and Kolb et al.;
6. Claims 1-10, 12, 14, 18, 20, 21, 25, 28 and 30-34 and 41 are rejected under 35 U.S.C. §103, as allegedly being obvious over Mathor et al. in view of each of Felts et al.; Wang et al.; Zhou et al. and Inaba et al., in further view of Naldini et al.

Applicant notes that all amendments and cancellations of Claims presented herein are made without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's

Patent Business Goals (PBG),[1] and without waiving the right to prosecute the amended or cancelled Claims (or similar Claims) in the future.

Applicant summarized the Interview in their previous response and incorporate that summary herein.

The rejections listed above are addressed in order below.

1. Double patenting.

Applicants have filed a terminal disclaimer over the cited patents.

2. The claims are not obvious over Mathor, Felts, Wang, Zhou and Inaba.

Claims 1-10, 12, 14, 18, 20, 21, 28, 30-34, and 41 are rejected under 35 U.S.C. §103, as allegedly being obvious over Mathor et al. in view of each of Felts et al.; Wang et al.; Zhou et al. and Inaba et al. Applicants respectfully traverse.

a. The Examiner has not properly considered the claim limitations

The Examiner alleges at page 17 of the Office Action that "based on the teachings of the art as a whole, one of skill in the art would have known that high MOI could be used to obtain cells with high numbers of proviral copies in their genome." Applicants respectfully disagree.

As a preliminary matter, this conclusion by the Examiner does not consider the claims and the data in the specification. The claims require that multiple transductions at high MOI be carried out and then that cell lines with 20 to 100 copies of the integrated vector be selected. The prior art does not teach that the claimed number of integrations (i.e., 20 to 100) can be achieved by a single high MOI transduction. Thus, contrary to the Examiner's assertion, one of skill in the art would not recognize that the claimed number of integrations can be achieved by a single high MOI transduction. The Examiner additionally argues that "even the prior teaches using MOI as high as 100 for efficient and stable transduction, without detrimental effects to the cells (see Wang et al. above). All of the references above demonstrate that the art does not discourage to use high MOI to transduce cells in vitro." Office Action, p. 16. Again, the

1 65 Fed. Reg. 54603 (Sept. 8, 2000).

Examiner has ignored that the claims require multiple transductions at high MOI. Following these multiple transductions at high MOI, the claims require selection of cell lines with from 20 to 100 integrated vectors. As discussed in the next section, the prior art does not teach the selection of such cells lines.

b. From 20 to about 100 integrated vectors

The cited references, alone or in combination, do not teach or suggest claim element of selecting cells that have a genome comprising from 20 to about 100 integrated vectors. The Examiner admits at page 8 of the Office Action that Mathor et al. and Zhou et al. do not specifically teach a genome comprising from 20 to about 100 integrated vectors. The Examiner then states that Mathor does teach that protein expression is directly proportional to the integration events (i.e., copy number) and that the prior art as a whole teaches that there is a positive correlation between the MOI, integration events, and transduction efficient, citing Felts and Wang. However, none of the these references teach the claimed limitation of more than 20 integrated vectors and thus the references, alone or in combination, do not teach each element of the claims.

Dr. Bleck specifically addressed the data contained in Mathor in paragraph 11 of his declaration:

> The data [in Mathor] shows that at 8 integrations, 1140 ng/10^6 cells/day of protein is produced, and that when 15 integrations were obtained, the protein production decreased to 1014 ng/10^6 cells/day or protein produced. This indicates that protein production had reached a plateau and that further introduction of retroviral vectors did no good or decreased protein production. Thus, one of skill in the art would conclude from the data additional integration past 8 integrations were not needed or not desirable.

At page 19 of the Office Action, the Examiner responds to Second Bleck Declaration and argues that Table 1 of Mathor et al. shows the result obtained with only one keratinocyte clone for each of the 8 and 15 integration events. Based on this observation, the Examiner then states:

> Such results cannot be extrapolated to all clones. The art teaches that retroviral insertion is random and that expression level is dependent on the insertion sites (see Mathor et al., p. 10376, column 1; Liu et al., Anal Biochem, 2000, 280:20-28, Abstract, p. 21, column 1; Stamps et al., Int J. Cancer, 1994, 57:865-874, Abstract, p. 868, column 1, p. 869, Fig. 2). Based on these references, one of skill in the art would expect clones with the same number of copies to have different expression levels, and therefore, would know to select multiple clones and look for the high expressing ones.

Applicants respectfully submit that this is sheer speculation by the Examiner and that it is the Examiner that is making an unsupported extrapolation of the data, not the applicants. There is no other data except for the clones identified in Table 1 of Mathor. It is this data that is addressed by Dr. Bleck. The data shows that the expression from cells with 15 integrated vectors decreased as compared to cells with 8 integrated copies. This fact cannot be disputed. It is the Examiner that is extrapolating the data, not the applicants. **There is no basis in this data for the Examiner to conclude that a person of skill in the art would be motivated to make cells lines containing more than 20 integrated vectors and select for high expressing clones.** In effect, the Examiner ignores the actual data and proceeds to extrapolate the data to support an argument that a person of skill in the art would be motivated to make cell containing 20 integrated retroviral vectors when the data set provides no evidence to support that conclusion. As stated by the Examiner at p. 14 of the Office Action, "An explanation does not equal evidence."

As Dr. Bleck states in his Second Declaration, at most, a person of ordinary skill in the art, considering Mathor, would conclude that protein expression is correlated to integration number only through about 8 integration events. Neither Felts nor Wang nor any of the other references cited by the Examiner provide evidence to the contrary. The Examiner has provided no evidence from which it can be concluded that a person of skill in the art would extrapolate the actual Mathor data to conclude that making cell lines with genomes containing greater than 20 integration events were desired or feasible. Indeed, the evidence, i.e., data, in Mathor argues otherwise as established in the Second Bleck Declaration.

c. Internal promoters

The claims have been amended to recite the use of promoters that are internal to the retroviral 5' and 3' LTRs. At pages 18-19 of the Office Action, the Examiner states that:

> With respect Zielske et al. they teach that, regardless of the copy number, there is a practical limit in the degree of gene expression which can be achieved with their retroviral vector in the particular cell they use due to the presence of the CMV promoter in their vector as opposed to the MLV vector of Kustikova et al., which does not have the CMV promoter and thus can attain increasing levels of transgene expression with increased copy numbers (p. 926, column 2, p. 929, column 1 third paragraph). Therefore, since the rejection is based on references teaching a vector which does not have the CMV promoter, this argument is not found persuasive.

Zielske et al., p. 929, col. 1, para. 3, teaches that:

> These data show a positive correlation between integration and baseline transgene expression and are in general agreement with data by Kustikova et al. However, in our model, we find that transgene expression reaches a plateau above 4 copies per cell. The reasons for this difference are not immediately obvious. The Kustikova study utilized a retroviral vector based on MLV, while ours uses an HIV-based vector with an internal CMV promoter. The differences could reflect a limit to available transcription factors compared to the MLV LTR.

The claims now recite the use of an internal promoter. The Examiner has admitted that the rejections do not apply to the use of internal promoters such as CMV. Zielske clearly teaches that use of internal promoters such as CMV results in a plateau of expression at 4 copies per cell. Thus, Applicants claimed invention where multiple copies of the retroviral vector are introduced via multiple transductions and wherein the vectors comprise an internal promoter driving expression of a desired gene is unexpected in view of the art.

When viewed as a whole, as required by the law, the prior art establishes that one of skill in the art would not have been motivated to make the presently claimed invention based on the teaching of the art. In particular, based on the teachings of the art relied on by the Examiner, one of skill in the art would not have been motivated to make cells lines comprising multiple integrated retroviral vectors comprising an internal promoter operably linked to a gene of interest. The art teaches that this would be futile.

d. The Examiner has not considered the prior art as a whole

The Examiner has failed to consider the prior art as whole. "The test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art, and all teachings in the prior art must be considered to the extent that they are in analogous arts. Where the teachings of two or more prior art references conflict, the examiner must weigh the power of each reference to suggest solutions to one of ordinary skill in the art, considering the degree to which one reference might accurately discredit another." MPEP 2143.01 II. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. MPEP 2143.01 III. *Citing KSR International Co. v. Teleflex Inc.*

Applicants respectfully submit that what the Examiner has done in this case is to rely on

teachings in references that allegedly support the Examiner's position while dismissing the teachings in references that are inconsistent with the Examiner's positions. When viewed as a whole, as required by the law, the prior art establishes that it was not predictable that multiple transductions at high MOI could be used to make viable cell lines containing more than 20 integrated vectors and expressing a protein of interest could be obtained. The results obtained by Applicants simply were not predictable and an obviousness rejection over the cited references is not proper. *See* MPEP 2143.01 III.

There are multiple examples of the fact that the Examiner has chosen to ignore the inconsistent teachings of the prior art and thus has failed to consider the teachings of the prior art as a whole.

As one example, the Examiner states "Applicant argues that malignant transformation of cells in vitro is almost certain to affect the production of the desired protein. Again, this is an assertion not supported by evidence." Office Action, p. 17-18. This statement was made in relation to the discussion of Coffin et al. in the Second Bleck Declaration. The Examiner has made several errors with respect to the Second Bleck Declaration. First, this passage by the Examiner mischaracterizes the actual evidence in Second Bleck Declaration. The Second Bleck Declaration is not limited to "malignant transformation." In contrast, Paragraph 5 of the Second Bleck Declaration establishes that:

> Coffin et al. confirms the teaching of Arai et al. that the incorrect use of retroviral vectors can lead to insertional mutagenesis. Furthermore, the Examiner's assumption that malignant transformation or other mutagenesis would not impede an immortalized mammalian cell from producing a protein of interest has no scientific basis. In fact, if an immortalized mammalian cell is mutagenized or transformed in some way by the vector, it is almost certain that production of the desired protein would be affected. The recombinant protein production industry relies on the use of standardized immortalized mammalian cells whose growth is predictable. Cells with additional mutations would be highly undesirable.

Thus, the Bleck Declaration established that cells containing additional mutation would be highly undesirable to the recombinant protein production industry. The Examiner has failed to address this evidence.

Second, the Bleck Declaration is evidence of what one of skill in the art would conclude based on Arai and Coffin (as well as the other references addressed) and cannot be summarily dismissed by the Examiner. Thus, contrary to the Examiner's assertion, Applicants have

submitted evidence to support their arguments. As held in *In re Sullivan*, 498 F. 3d 1345, 1351, 81 USPQ2d 1034 (Fed. Cir. 2007):

> Rebuttal evidence is "merely a showing of facts supporting the opposite conclusion." *In re Piasecki*, 745 F.2d 1468, 1472 (Fed.Cir.1984). Evidence rebutting a *prima face* case of obviousness can include: "evidence of unexpected results," *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1369 (Fed.Cir.2007), evidence "that the prior art teaches away from the claimed invention in any material respect," *In re Peterson*, 315 F.3d 1325, 1331 (Fed.Cir.2003), and evidence of secondary considerations, such as commercial success and long-felt but unresolved needs, *WMS Gaming, Inc. v. Int'l Game Tech.*, 184 F.3d 1339, 1359 (Fed.Cir.1999).

Id. Importantly, when a patent applicant puts forth rebuttal evidence, the Office must consider that evidence. *Id., see also In re Soni*, 54 F.3d 746, 750 (Fed.Cir.1995) (stating that "all evidence of nonobviousness must be considered when assessing patentability"); *In re Sernaker*, 702 F.2d 989, 996 (Fed.Cir.1983) ("If, however, a patent applicant presents evidence relating to these secondary considerations, the board must always consider such evidence in connection with the determination of obviousness."). The Second Bleck Declaration provides evidence concerning the prior art that the Examiner has failed to consider or address. Thus, the Examiner has not considered the prior art as a whole.

As another example, the Second Bleck Declaration establishes that Walker et al. teaches that retroviruses and repeated genes are often silenced or suppressed by mammalian cells. Because of viral interference and gene silencing or suppression, a person of ordinary skill in the art would be discouraged from using sequential transductions to increase viral inert number and would be discouraged from attempting to create immortalized mammalian cell lines with the claimed number of insertions. In response to this evidence, the Examiner argues that Walker:

> is related to transducing a single cell with two distinct retroviral vectors (i.e., vectors based on Murine Moloney Sarcoma Virus and Harvey virus) and demonstrate that simultaneous retroviral transduction (i.e., with both vectors) was infrequent; Walker et al. conclude that transduction of the cell with one viral vector type interferes with the cell being transduced by another vector type, i.e., their teachings are applicable when transducing the same cells with two distinct vector types (Abstract, Overview Summary, p. 1137, column 1). Such teaching is irrelevant for the claimed invention, which is drawn to transduction with a single retroviral vector type, and therefore, interference from another vector is not a problem.

Office Action, p. 20.

Applicants respectfully submit that the Examiner has not considered the entire reference. Walker does teach, as the Examiner notes, transduction of the cell with one viral vector type interferes with the cell being transduced by another cell type. However, Walker goes on to teach at p. 1137, column 2, that the prior art recognized that "viral interference resulted when susceptible cells were rendered resistant to specific retroviral infections by preinfection with a virus bearing the same glycoprotein specificity (Weiss, 1984). . . .This is thought to occur because the leukemia virus particles bear envelope proteins similar to sarcoma virus envelope glycoproteins, which competitively block the cell receptors and prevent binding by RSV viral particles." After ruling out this type of interference in their study, Walker et al. concluded that "The data suggest that the interference we observed with sequential retroviral transductions may occur at the level of retroviral DNA integration and or expression. Possibly retroviral DNA integration is not as random as currently thought." Walker et al., p. 1137, column 2.

Thus, what Walker et al. were testing was whether the same viral interference observed when vectors with similar glycoprotein specificities are used in a transduction protocol would be observed when vectors with different glycoprotein specificities were used. They not only found that viral interference existed, but that quite likely the interference existed at the level of integration and or expression. Thus, a person of skill in the art would recognize that these findings are applicable to situations where vectors with the same glycoprotein specificity are used (which applies to use of the same vector) as well as to situations where different vectors are used.

As still another example, the Examiner argues that:

> With respect to Bestor, the reference is related to silencing in vivo and not cells in vitro. For example, Bestor teaches that, while fibroblasts transduced with retroviral vectors stably expressed adenosine deaminase in vitro, transplantation of these cells into mice resulted in decreased adenosine deaminase expression (p. 409, column 2, last paragraph.

This is only one example from Bestor. Bestor generally teaches that:

- In mammals, the insertion of retroviral DNA or the incorporation of repeat arrays can trigger transcriptional silencing of the inserted sequences, usually via mechanisms that involve methylation of DNA within regulatory regions. P. 409, column 1.

- I will argue here that gene silencing mechanisms are diverse and efficient and are likely to represent a barrier to many forms of gene therapy. Id.
- The existence of gene silencing, the recognition and inactivation of alien genes by target cells (reviewed in ref. 1), has only recently been recognized as an additional challenge to gene therapy. Id.
- Many cases are known in which a transferred gene undergoes a brief period of expression followed by a decline to undetectable levels without the loss of the expression construct. Id.
- Repeat-induced gene silencing has clear relevance for any gene therapy approach that is likely to lead to the insertion of multicopy arrays. P. 410, column 1.
- Gene silencing can also occur at the RNA level even while transcription proceeds at high rates. P. 410, column 2.
- It should be noted that the mechanisms involved in virtually every form of gene silencing remain to be discovered, and research in this area is likely to accelerate in the near future. P. 411, column 1.

Applicants further note that the example cited by the Examiner is derived from Palmer et al., Proc. Nat'l. Acad. Sci. USA 88:1330-34 (1991). Applicants have attached this reference to this response for the Examiner's convenience. Applicants notes that Palmer et al. does not address copy number of the retroviral vector and thus does not address the statements in Bestor that relate to silencing of multiple copies of retroviral vectors, or just the introduction of multiple copies of the same gene, regardless of vector. A person of skill in the art would recognize that those statements are far more applicable to the state of the prior art on introduction of multiple genes into a host cells as is presently claimed. The import of these statements is clear: there was a great deal of concern in the prior art that gene silencing would limit the effectiveness of the introduction of multiple copies of a retroviral vector, or indeed, any vector into a target cell. Applicants note that this consistent with Mathor et al., which shows that expression decreased in cells with 15 copies of a vector as compared to cells with 8 copies of a vector. Mathor shows that increasing copy number past a certain point resulted in a decrease in expression.

As a final example, the Examiner continues to rely on Kustikova et al. and Zielske et al.

to rebut Applicants arguments based on Arai and Coffin, even though it is admitted that these references are not prior art. Office Action, p. 13. In spite of this admission, the Examiner continues to rely on Kustikova and Zielske to attempt to rebut the Applicants arguments and find the claims obvious. Applicants note the content of the prior art must be analyzed as it existed "at the time the invention was made" to avoid impermissible hindsight. MPEP 2141.01 III. It simply is not proper to use a reference that is not prior art to rebut Applicants arguments regarding the scope and content of the prior art at the time the invention as made. However, this is what the Examiner continues to do. As stated by the Examiner:

> However, these post-filing references were cited to demonstrate that, contrary to Applicant's assertions, one of skill in the art would not have been discouraged by the teachings of Arai et al. and Coffin et al. to obtain higher integration events by increasing the MOI.

Applicants arguments based on Arai and Coffin relate to the scope and content of the prior art as of the priority date of the application. It is contrary to both the MPEP and the established precedent of the Supreme Court to use references published after the invention was made to rebut such arguments. Effectively, the Examiner has made a post-filing date reference part of the scope and content of the prior art. This is not proper.

e. The claims are not obvious

To sum up, none of the prior art references cited by the Examiner, alone or in combination, teach a method where multiple transductions at a high MOI are used to make cells and then the cells are selected for clones containing from 20 to about 100 integrated retroviral vectors. Moreover, none of the references, alone or in combination, teach methods of making cells lines comprising multiple integrated retroviral vectors comprising an internal promoter operably linked to a gene of interest. Accordingly, the Examiner has not established a prima facie case of obviousness. The primary reference cited by the Examiner is Mathor. Mathor teaches at most a cell with 15 integrated retroviral vectors. The remaining references do not teach or suggest the claimed methods of making cells containing the claimed number of integrated vectors. In fact, references such as Arai, Coffin, Walker and Bestor teach that it would not be advisable to seek to make cells containing the claimed number of vectors for a variety of reasons explained in detail above. At the very least, these references establish the

unpredictability associated with making cells containing high numbers of integrated vector and that the prior art certainly was not in agreement that such cell lines would be viable or useful. As indicated above, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. MPEP 2143.01 III. *Citing KSR International Co. v. Teleflex Inc.* Here, modification of Mathor with the other references does not provide predictable results. Accordingly, Applicants request that this rejection be withdrawn.

3. The claims are not obvious over Mathor, Felts, Wang, Zhou, Inaba and Burns.

Claims 1-10, 12, 14-18, 20, 21, 28, 30-34, and 41 are rejected under 35 U.S.C. §103, as allegedly being obvious over Mathor et al. in view of each of Felts et al.; Wang et al.; Zhou et al. and Inaba et al. in further view of Burns et al. This combination of references (i.e., the addition of Burns et al.) does not cure the deficiencies noted for the combination of Mathor, Felts, Wang, Zhou and Inaba. Burns et al., alone or in combination with the other cited references, does not teach or suggest a method where multiple transductions at a high MOI are used to make cells and then the cells are selected for clones containing from 20 to about 100 integrated retroviral vectors or methods of making cells lines comprising multiple integrated retroviral vectors comprising an internal promoter operably linked to a gene of interest. Applicants respectfully request that this ground of rejection be withdrawn because the Examiner has not established a prima facie case of obviousness.

4. The claims are not obvious over Mathor, Felts, Wang, Zhou, Inaba and Schroder.

Claims 1-10, 12, 14, 18, 20, 21, 26, 28, 30-38 and 41 are rejected under 35 U.S.C. §103, as allegedly being obvious over Mathor et al. in view of each of Felts et al.; Wang et al.; Zhou et al. and Inaba et al., in further view of Schroder et al. This combination of references (i.e., the addition of Schroder et al.) does not cure the deficiencies noted for the combination of Mathor, Felts, Wang, Zhou and Inaba. Schroder et al., alone or in combination with the other cited references, does not teach or suggest a method where multiple transductions at a high MOI are used to make cells and then the cells are selected for clones containing from 20 to about 100 integrated retroviral vectors or methods of making cells lines comprising multiple integrated

retroviral vectors comprising an internal promoter operably linked to a gene of interest. Applicants respectfully request that this ground of rejection be withdrawn because the Examiner has not established a prima facie case of obviousness.

5. The claims are not obvious over Mathor, Felts, Wang, Zhou, Inaba and Primus and Kolb.

Claims 1-10, 12, 14, 18, 20-24, 26, 28, 30-34, and 39-41 are rejected under 35 U.S.C. §103, as allegedly being obvious over Mathor et al. in view of each of Felts et al.; Wang et al.; Zhou et al. and Inaba et al. in further view of Primus and Kolb et al. This combination of references (i.e., the addition of Primus and Kolb et al.) does not cure the deficiencies noted for the combination of Mathor, Felts, Wang, Zhou and Inaba. Primus and Kolb, alone or in combination with the other cited references, does not teach or suggest a method where multiple transductions at a high MOI are used to make cells and then the cells are selected for clones containing from 20 to about 100 integrated retroviral vectors or methods of making cells lines comprising multiple integrated retroviral vectors comprising an internal promoter operably linked to a gene of interest. Applicants respectfully request that this ground of rejection be withdrawn because the Examiner has not established a prima facie case of obviousness.

6. The claims are not obvious over Mathor, Felts, Wang, Zhou, Inaba and Naldini.

Claims 1-10, 12, 14, 18, 20, 21, 25, 28 and 30-34 and 41 are rejected under 35 U.S.C. §103, as allegedly being obvious over Mathor et al. in view of each of Felts et al.; Wang et al.; Zhou et al. and Inaba et al., in further view of Naldini et al. This combination of references (i.e., the addition of Naldini et al.) does not cure the deficiencies noted for the combination of Mathor, Felts, Wang, Zhou and Inaba. Naldini et al., alone or in combination with the other cited references, does not teach or suggest a method where multiple transductions at a high MOI are used to make cells and then the cells are selected for clones containing from 20 to about 100 integrated retroviral vectors or methods of making cells lines comprising multiple integrated retroviral vectors comprising an internal promoter operably linked to a gene of interest.

Applicants respectfully request that this ground of rejection be withdrawn because the Examiner has not established a prima facie case of obviousness.

CONCLUSION

All grounds of rejection and objection of the Office Action of October 2, 2008 having been addressed, reconsideration of the application is respectfully requested. It is respectfully submitted that the invention as claimed fully meets all requirements and that the claims are worthy of allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

Dated: March 2, 2009

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